UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,873	09/05/2003	Shyam S. Mohapatra	USF-182XC1	6872

23557 7590 09/20/2007

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER
NOBLE, MARCIA STEPHENS

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/655,873	MOHAPATRA ET AL.	
	Examiner	Art Unit	
	Marcia S. Noble	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6-9,11,12,15,18,19,43,45-50,52-58,60,62,64,66 and 68-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6-9,11,12,15,18,19,43,45-50,60,62,64,66,68-73 and 52-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Matters

1. The supplemental amendments to the specification, sequence listing, and CRF, filed 7/5/2007 are acknowledged. The CRF was entered and accepted on 7/15/2007.

Status of Claims

2. Claims 1-4, 6-9, 11, 12, 14, 15, 18-21, 23-31, 43-50, and 52-68 are pending. Claims 1, 3, 6-8, 15, 18, 43, 45-48, 50, 53-58, 60, 62, 64, and 68 are amended, claims 2, 4, 14, 20, 23-31, 44, 59, 61, 63, 65, and 67 are canceled, and claims 69-73 are newly added by amendment 6/26/2007. Claims 1, 3, 6-9, 11, 12, 15, 18, 19, 43, 45-50, 52-58, 60, 62, 64, 66, and 68-73 are under consideration.

Information Disclosure Statement

3. The information disclosure statement (IDS) was submitted on 2/23/2007 The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The information disclosure statement (IDS) submitted on 6/26/2007 was filed after the mailing date of the Non-Final Office Action on 2/26/2007. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 54-57, 69, and 70 as amended or newly added are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. {Hogan et al. (1998) Eur. J. Immunol. 28: 413-423}, and further in view of Li et al. {Li. et al. (1996) J. Immunol. 157: 3216-3219} and further in view of US patent 6,693,086

(2.17.2004) priority to (6.25.1998), hereafter referred to as Dow et al, and O'Donnell et al. {O'Donnell (1999) J. Immunol. 163:4246-4252}. The rejection is maintained for reasons of record set forth in the Non-Final Action, mailed 6/5/2006 at pages 4-6, which states the instantly cited art renders the claimed pharmaceutical composition comprising the IL12 vector, the IFN-gamma vector and an antigen obvious.

Applicant traverses this rejection on the following grounds:

Applicant asserts that Hogan et al teaches that the use of IL-12 gene alone was far superior to gene transfer with IL-12 and IFN-gamma (p. 12 of remarks filed 6/26/2007) and therefore teaches away from the art. Applicant's argument is not found persuasive because the prior art reference must be considered as whole for its teachings. Although Hogan et al may have found in their experiments that IL-12 was more effective, they also teach the combined effect of IL-12 and IFN-gamma that results in an immune response is functional and has been used in the art. The disclosure of an alternative in itself that is more effect or less effective does not constitute "teaching away" an alternative because a factor of effectiveness does not discredit the use of the less effective embodiment. See In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). See also MPEP §2123. Therefore, composition comprising these two vectors would still be considered obvious.

Applicant also asserts that Hogan et al uses viral vectors and Li et al and Dow et al use liposome mediated vectors for their respective gene therapies, which is different from the use of plasmid vectors in the instant invention.

Applicant asserts that Dow et al teaches away from the use of naked DNA delivery and use of viral vectors as being far less effective than the liposome mediated plasmid delivery used by Dow et al. (p. 12-13 of remarks filed 6/26/2007). These arguments are not found persuasive because again a factor of one alternative being more or less effective over another alternative does not constitute teaching away from use or combining the art. Dow et al and Li et al both establish that plasmid with or without the use of a liposome have been used in the art sucessfully in gene transfer for eliciting an immune response as has been shown by Hogan et al and therefore use of a plasmid vector would be an obvious variant of the composition comprising gene therapy plasmid vectors with IL-12 and IFN-gamma.

Applicant also asserts that with regards to claims 68, the combination of references wouldn't necessarily produce the same predictable result. Hogan et al teaches that treated mice had IgG2a antibody levels that were similar to those found in controls and that this is different than those found in the instant invention and therefore claims 54-57 and 68 are not obvious. Applicant's arguments are not found persuasive because as previously stated in the Office Action, mailed 2/26/2007 (p. 4-5), "In considering a product, such as the claimed composition comprising a IL-12 expression vector, an IFN-gamma vector and an antigen, its patentability **does not** depend upon the manner by which the product was produced or used (See MPEP 2113.). The claimed pharmaceutical composition of the instant invention is results increases Th1-type cytokine production, increases IgG2a, decreases Th2-type production and reduces serum IGE when

administered to a patient *in vivo*. If the same components of a composition are present, then composition should function in the same manner, even if it is not stated directly in the art that discloses the composition. Therefore, the means of use or effects of the composition does not carry patentable weight."

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

5. The rejection of claims 2-4, 6, 7, 8, 45-48, 50, under 35 U.S.C. 112, first paragraph, as containing new matter in the recitation "the administering step includes selecting", is withdrawn.

Applicant amended the claims to remove this recitation and therefore the rejection is withdrawn.

Scope of Enablement

6. Claims 1, 3, 6-9, 11, 12, 15, 18, 19, 43, 45-50, 52-58, 60, 62, 64, 66, and 68-73 as amended, previously presented, or new added, are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for:

A method of modulating an immune response comprising administering by intramuscular injection to a patient an effective amount of pharmaceutical composition comprising a nucleic acid encoding the nucleic acid sequence of SEQ ID NO:7, which encodes the p35 subunit of human IL-12, and the nucleic acid sequence of SEQ ID NO:9, which encodes the p40 subunit of human IL-12 both operably linked to a promoter capable of driving expression of said nucleic acid and the nucleic acid sequence of SEQ ID NO:11, which encodes human IFN-γ, operably linked to a promoter capable of driving expression of said nucleic acid, and administering an antigen subcutaneously, wherein the administration of said composition and said antigen results in an increase of Th1-type cytokines INF-γ and IL-2, an increase in the levels of IGg2a specific to said antigen, a decrease of Th2-type cytokine IL-2, and reduced serum IgE levels;

And while being enabled for:

A pharmaceutical composition comprising a nucleic acid encoding the nucleic acid sequence of SEQ ID NO:7, which encodes the p35 subunit of human IL-12, and the nucleic acid sequence of SEQ ID NO:9, which encodes the p40 subunit of human IL-12 both operably linked to a promoter capable of driving

expression of said nucleic acid and the nucleic acid sequence of SEQ ID NO:11, which encodes human IFN-γ, operably linked to a promoter capable of driving expression of said nucleic acid,

does not reasonably provide enablement for:

A method comprising administering 1) any nucleic acid sequence encoding IL-12, a promoter operably linked to any nucleic acid or protein, any nucleic acid sequence encoding any IFN-γ, a promoter operably linked to any nucleic acid or protein, and an antigen, 2) administering by any route of administration, 3) administering the two nucleic acids independently, wherein the administering step involves a selection step, 4) and wherein the administration results in an increase in any or all Th1-type cytokine production, an increase in any or all IgG2a, a decrease in any or all Th2-type cytokine production, and a decrease in IgE levels;

and does not reasonably provide enablement for:

A pharmaceutical composition comprising any nucleic acid sequence encoding IL-12, a promoter operably linked to any nucleic acid or protein, any nucleic acid sequence encoding any IFN-γ, a promoter operably linked to any nucleic acid or protein, and an antigen.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Applicant traverses this rejection on the following grounds:

Applicant asserts that specification need not teach how to use and make every embodiment of an inventions because the artisan's knowledge of the prior art and routine experimentation can often fill in the gaps. Applicant further provides several arts, such as US Pat No 6,475,995, Warner and Lu, and US Pat No 6, 710,035 to demonstrate that multiple routes of administering a gene transfer vector for immunotherapy have been taught in the art. These arguments are not found persuasive because these routes of administration mainly pertain to methods in the mouse and as Van Drunen Little can den Hurk et al previously stated, "Although the concept of DNA immunization has proven to be extremely successful in inducing immune responses in mice, significant barriers exit to effective induction of immunity in large animals and humans using DNA immunization." (see p. 114). The claims more broadly encompass DNA immunization with other species and as previously suggested routes of administration are still unpredictable in the art. The specification does not teach a means to overcome these unpredictabilities. Therefore, the method is not enabled for routes of administration taught outside of the specification.

Applicant asserts that the art of Van Drunen Littel van den Hurk et al and Scheerlinck suggest that co-administration with cytokines might enhance or modulate DNA vaccination and they suggest that the art of Gautam et al and Yang et al are nor applicable to the instant invention because they do no address treating with cytokines to elecit an immunological response. These arguments are not found persuasive because these art were not relied upon to teach specifically DNA vaccination with vectors encoding cytokines. They were used to

establish that various routes of administration of gene transfer vectors have many complications in the art and demonstrate that the art of gene transfer is unpredicatable because of the various complication associated with gene vector delivery described in the art. Therefore, it is not relevant that these arts did not specifically teach the cytokine administration or gene transfer of cytokine gene to elicit an immune response.

With regards to whether cytokines IL-2, INF-gamma, and IL-4 disclosed by the specification would be representative of the Th1 and Th2 cytokines, Applicant asserts that the expression profiles disclosed in the specification represent the full breadth of Th1 and Th2 cytokine production. Applicant submits Wenner et al, Bradley et al, and Glimcher et al to demonstrate that IL-12 and INF-gamma stimulate Th1 differentiation that IL-4 promotes Th2 differentiation. These arguments and art have been fully considered but are not found persuasive. It is not being disputed, as demonstrated in Wenner, Bradley and Glimcher, that IL-12, INF-gamma, and IL4 are involved in the differentiation of Th1 and Th2 differentiation. However, as previously stated in the Office Action, mailed 2/26/2007 (p. 15), "the Th1 and Th2 type cytokines are genera of cytokines that have several known species members. However, the specification only discloses the use of IL-2 and INF-γ as examples of Th1 type cytokines and IL-4 as an example of Th1 cytokines. Because the novelty of the instant invention seems to be in the specific type of immune response being elicited, it is not clear that the expression profiles of one or two cytokines from each group would represent the full breadth of Th1-type cytokine production and th2-type cytokine production.

Therefore, because the other cytokines of the genera were not measured an artisan would not know if other Th1 and Th2 type cytokine expression profiles will be indicative of the claimed immune response. Therefore, because the specification only discloses IL-2, IFN-γ, and IL-4 expression profiles, the invention is only enabled for these specific cytokines." This is further supported by the art of Wenner et al (p. 1442, col 1), which states, "Despite the importance of IL-12 and IL-4, other cytokines also participate in controlling Th development of naïve T cells. IL-10 and IFN-gamma can contribute to T cell development through inhibition of APC." Therefore, because the art suggests that other cytokines play a role and because the novelty of the invention seems to rely upon the cytokine profiles, the instant invention is only enabled for the cytokine profiles demonstrated in the specification, IL-2, IFN-gamma, and IL-4.

Since Applicant's arguments and amendments to the claims have not be found persuasive to overcome the instant enablement rejection, these grounds of rejection are maintained.

Also, Applicant did not address all of the enablement issues made of record. As previously stated in the Office Action, mailed 2/26/2006 (p. 12), "The instant invention is drawn to an expression vector encoding "an amino acid sequence of" (such as claim 3 and 50) which encompasses any sequence encoding said amino acids, including fragments thereof. This will encompass a non-coding segments or short fragments of the amino acid sequence that do not have biological activity of IL12 or IFN-γ and therefore would not result in the Ig and cytokine expression profile claimed. Furthermore, the specification only

teaches the use of the full coding sequences of the p35 and p40 subunits of IL-12 or SEQ ID NOS:7 & 9 and the full IFN-γ gene sequence of SEQ ID NO:11, which comprise whatever biological active components necessary to obtain the claimed immune response. Because the specification does not disclose which fragments of these sequences are encoding the biologically active and functioning components of the sequences, an artisan would only know how to use or make the instant method and composition to obtain the claimed immune response using the full sequences disclosed."

Therefore, because these grounds of enablement have not been addressed, the by the amendments or Applicant's arguments, the instant invention for above disclosed reasons as well.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. The rejection of claims 1-4, 6-9, 11, 12, 14, 15, 18-21, 23-31, 43-50, and 52-68 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn.

Applicant amended the claims to clarify all of the 112 2nd paragraph issues of record; therefore, the rejection is withdrawn.

8. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcia S. Noble
AU 1632

PETER PARAS, JR.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600